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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,930	09/20/2005	Maria Alessandra Alisi	278220US0PCT	7516
22850	7590	02/19/2009		
OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			EXAMINER CHANG, CELIA C	
			ART UNIT 1625	PAPER NUMBER
			NOTIFICATION DATE 02/19/2009	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No. 10/549,930	Applicant(s) ALISI ET AL.	
	Examiner Celia Chang	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 25 November 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 and 33-35 is/are pending in the application.
- 4a) Of the above claim(s) 30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-29, 31 and 33-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/25/08</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Response filed by applicants dated Nov. 25, 2008 have been entered and considered carefully.

Claims 1-29, 31, 33-35 are pending. Claim 30 stayed withdrawn from consideration.

2. The inadvertent listing of the Suzuki reference is hereby corrected to US 6,906,746.

3. Applicant's arguments with respect to claim 1-29, 31, 33-35 have been considered but are moot in view of the new grounds of rejection based on newly available references.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

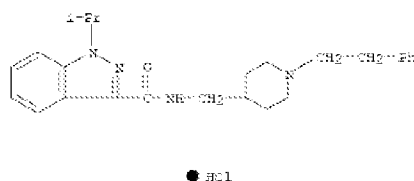
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-29, 31, 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alisi et al. US 6,197,769 supplemented with CA129:316219 in view of Catlow et al. US 5,654,320 (cited in previous office action) supplemented with CA125:275867.

Determination of the scope and content of the prior art (MPEP §2141.01)

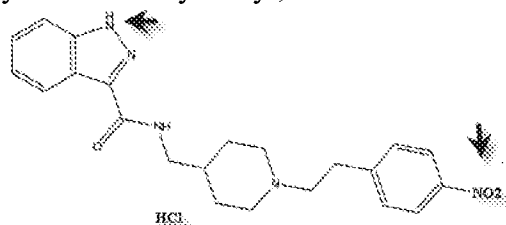
Alisi et al. '769 disclosed structural very close compound see RN 214851-35-1 delineated by CA129:

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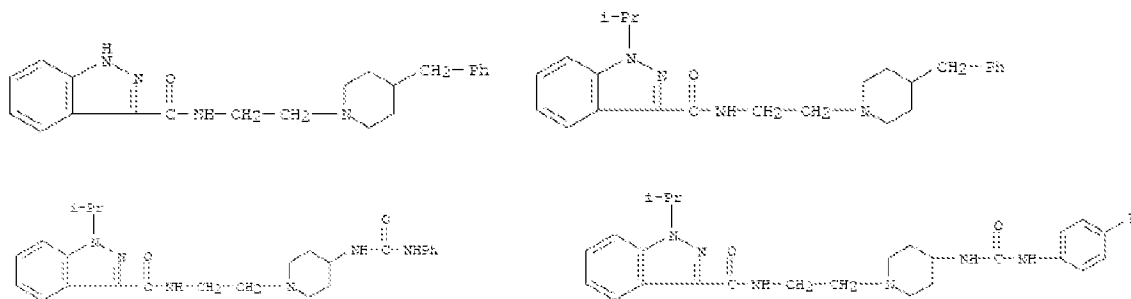


Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference of this species and the species of the claims for example claim 8, is that the Rb moiety of claim 8 is H, and the proviso condition requires that the terminal phenyl to be “substituted” by other than hydroxyl, i.e structure delineated in the response on page 4:



Catlow et al. ‘746 is analogous art wherein it taught that the Rb moiety is optional unsubstituted or substituted and the terminal phenyl is optionally substituted with non-hydroxyl substituents i.e.:



Finding of prima facie obviousness—rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art in possession of Alisi et al. ‘769 and Catlow et al. would be motivated to modify the Alisi et al. ‘769 compounds with attributes taught in analogous art since such attributes were not only generically taught in the Catlow et al. ‘746 reference they have been particularly disclosed to be operable for the biological activity.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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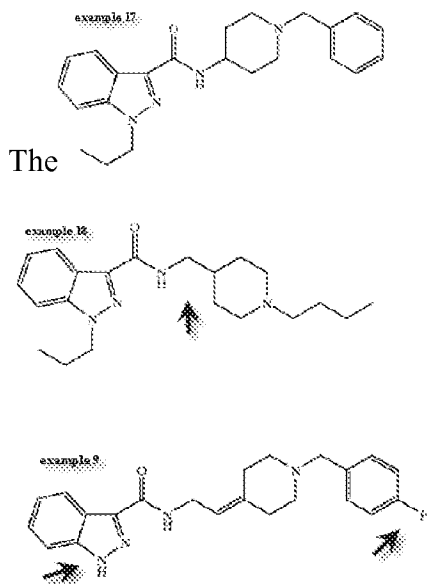
The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

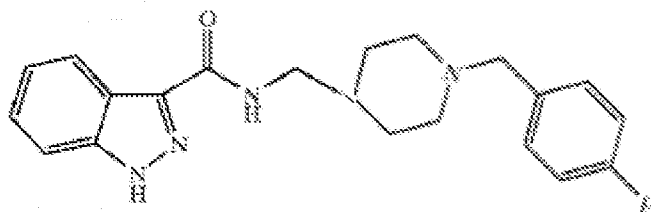
Claims 1-29, 31, 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suzuki et al. US 6,096,746 in view of Alisi et al. US 6,197,769.

Determination of the scope and content of the prior art (MPEP §2141.01)

Suzuki et al. '746 generically taught the indazolyl piperidine compounds and provided examples as following:



Thus, provided the clear guidance for the compound:

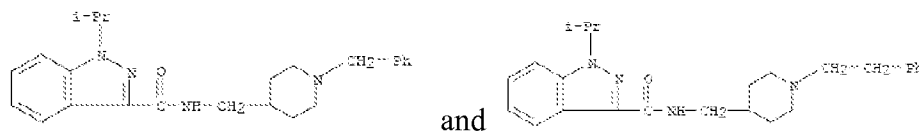


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Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the prior art teaching is that instead of a methylene chain, the claims are drawn to an ethylene linker.

Alisi et al. '769 disclosed



Therefore particularly pointed to the optional choices between the methylene and ethylene linker.

Finding of prima facie obviousness—rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art in possession of the above references are well aware of the teaching and attributes for the indazolylpiperidineyl 5HT4 active compounds. The modification of one group of conventional proven compounds by the attributes of another group of conventional proven compounds is prima facie obvious. The explicit compounds enabled for the generic teaching of the prior art teach, suggest and motivate one skilled in the art to employ the combined operable merits in making modification of one another which is the instant claims.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

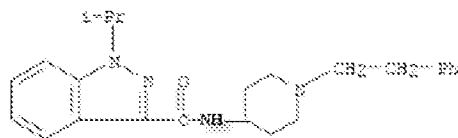
Claims 1-29, 31, 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schaus et al. (cited in previous office action) in view of Patani.

Determination of the scope and content of the prior art (MPEP §2141.01)

Schaus et al. disclose ethylene inserted compound as the claims.

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See p.1948, table 3, compound 19d which is:



Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

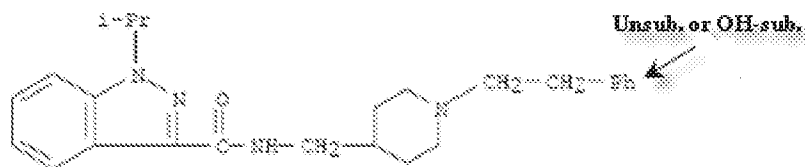
The difference between the above compound and the instant claims is that the linker between the indazolyl moiety and the piperidinyl moiety is CONH instead of the NHCO. The amide bond and the reverse amide bond have been known to be bio-isosteric structure (see Patani et al. p.3170 right column, table 48). Bioisosteric replacement has been known by medicinal chemists to be *the rational modification of lead compound* (see p.3147).

Finding of prima facie obviousness—rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would be motivated to employ the reverse amide for the lead compound 19d (see p. 1951 right column last paragraph) of Schaus et al. because the bioisosteric reverse amide modification is a design choice with reasonable expectation that the modified compound would have the merits and activity of the lead compound.

7. Claims 1-29, 31, 33-35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,197,769 in view of Patani et al.

US 6,196,769 claimed the compounds wherein the phenyl moiety is unsubstituted or optionally hydroxyl substituted i.e. the proviso condition:



The difference of the instant claims and the issued claims is that the unsubstituted or hydroxy substituted phenyl is combined with other amide bond linkers (NHCO or NHCOCH₂). The replacement of one amide bond bioisostere with another conventionally known amide bond isostere is prima facie obvious because biobioisosteric replacement is the rational design in medicinal chemistry. The same rational delineated supra is also applicable here and incorporated by reference.

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8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang, Ph. D. whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Feb. 10, 2009

/Celia Chang/
Primary Examiner
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